



BOLOGNA

17 FEBBRAIO 2023

NH De La Gare

POLICITEMIA VERA NEL 2023:

qualcosa è cambiato

Paziente che sviluppa NMSC recidivanti

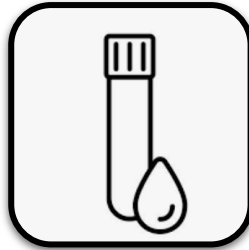
Camilla Mazzoni Istituto di Ematologia «L. e A. Seràgnoli», Università degli Studi di Bologna, IRCCS S. Orsola-Malpighi

No Disclosures

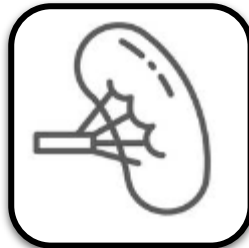


CLINICAL CASE – Jul 2005

MEN 68 years-old– Non smoker, IBD, hypertension, localized melanoma exeresis in 1983, right leg recurrent superficial venous thromboses



WBCs $7.3 \times 10^9/L$ (normal differential count), Hb 19.2 g/dl, Hct 59%, PLT $262 \times 10^9/L$, LDH within normal limit, normal iron deposits

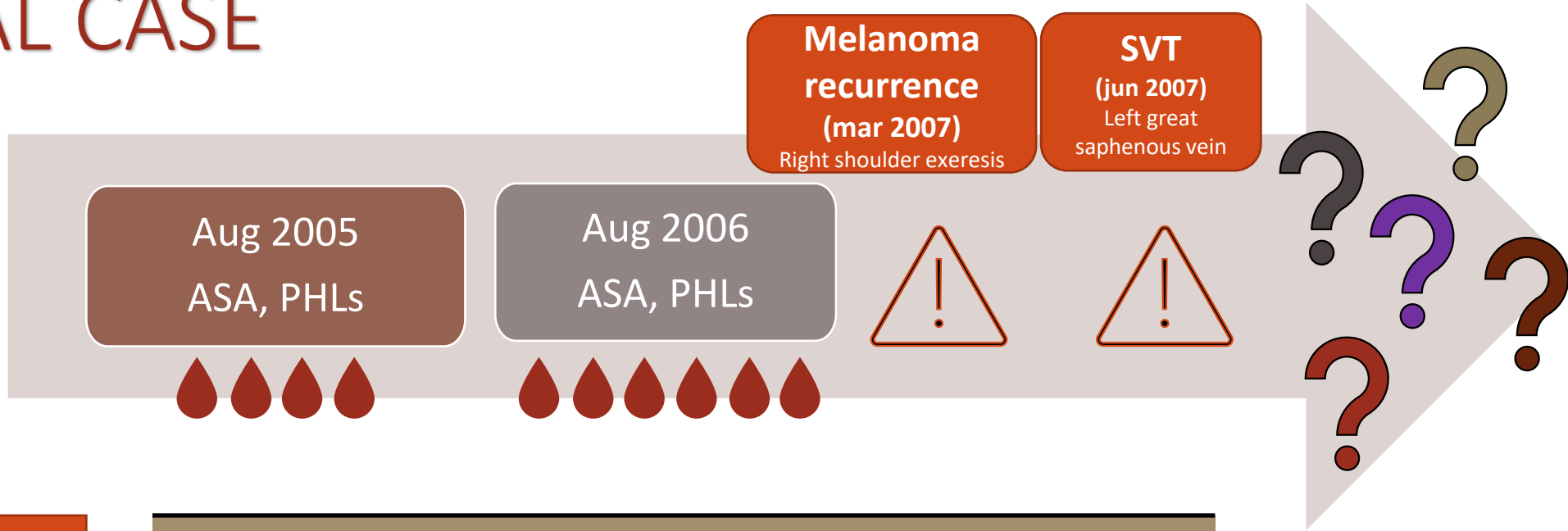


No hepato-splenomegaly



Face rubosis, no relevant symptoms

CLINICAL CASE



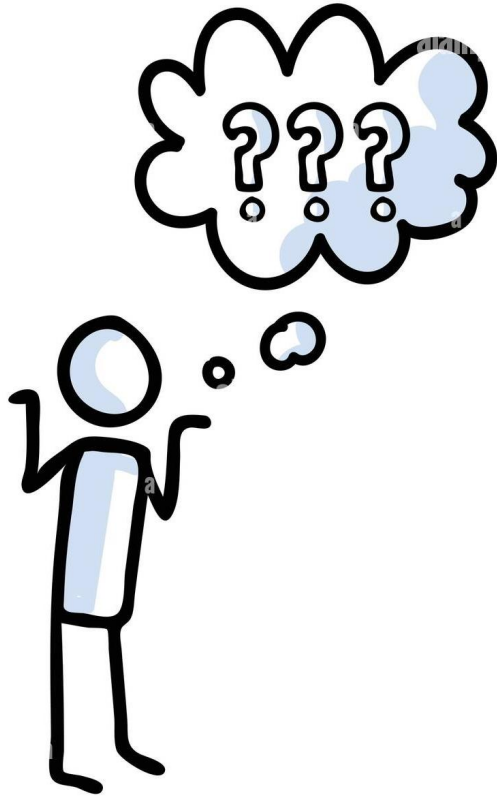
High risk PV

**Refuses
cytoreduction**

	Aug 2005 PV diagnosis	Aug 2006
WBC	7.86 k/ μ L	7k/ μ L
Hgb	18 g/dL	13.9 g/dL
PLTs	319 k/ μ L	554 k/ μ L
Hct	58%	44%
No of PHL/yr	4 (Aug-sep 2005)	6



CLINICAL CASE

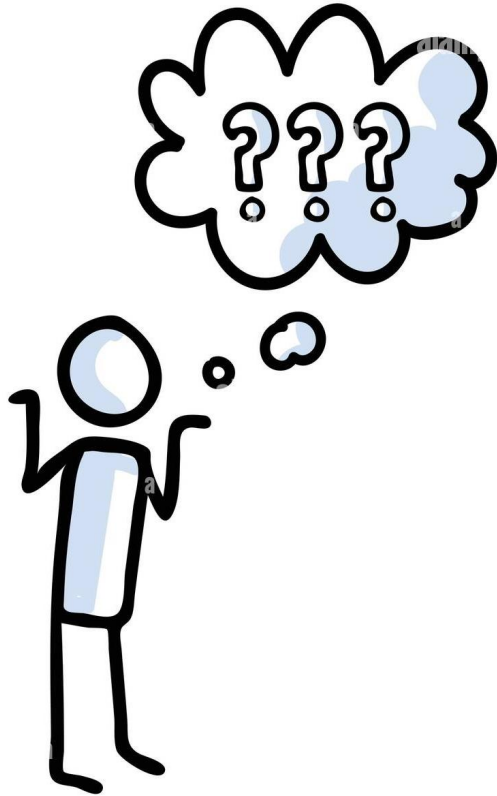


What to do next?

1. Nothing, just keep it up
2. Evaluation of JAK2, BMB and HU start
3. Evaluation of JAK2 and HU start (without BMB)



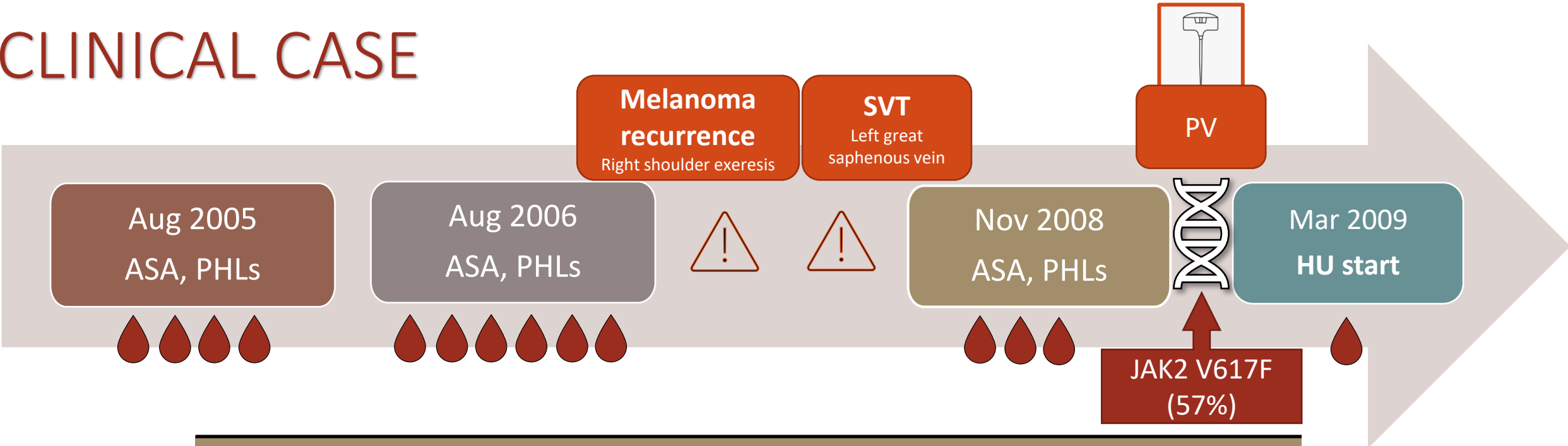
CLINICAL CASE



What to do next?

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2. **Evaluation of JAK2, BMB and HU start**
3. Evaluation of JAK2 and HU start (without BMB)

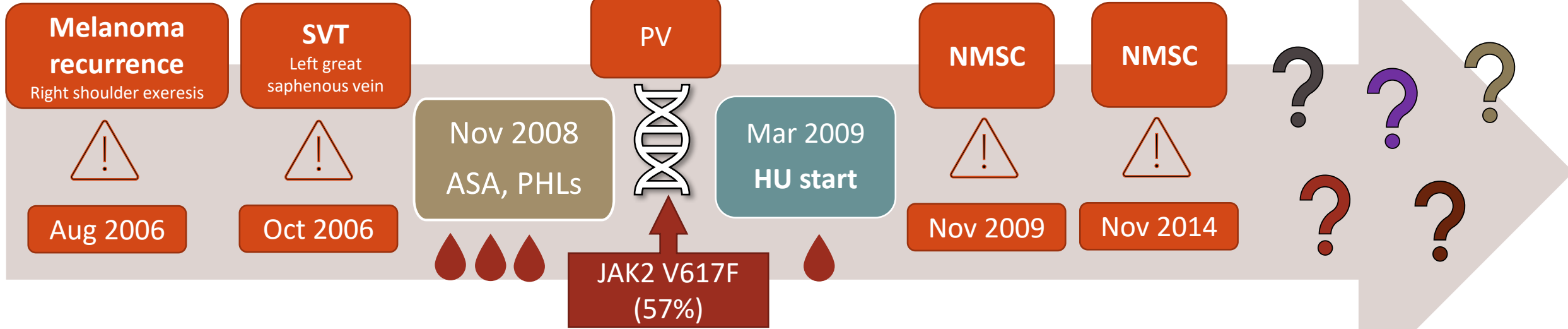
CLINICAL CASE



	Aug 2005	Aug 2006	Nov 2008	Mar 2009
WBC	7.86 k/ μ L	7k/ μ L	15.8 k/ μ L	17.8k/ μ L
Hgb	18 g/dL	13.9 g/dL	12.8 g/dL	13.5 g/dL
PLTs	319 k/ μ L	554 k/ μ L	359 k/ μ L	413 k/ μ L
Hct	58%	44%	47%	43%
No of PHL/yr	4 (Aug-sep 2005)	6	3	1 (3 months)

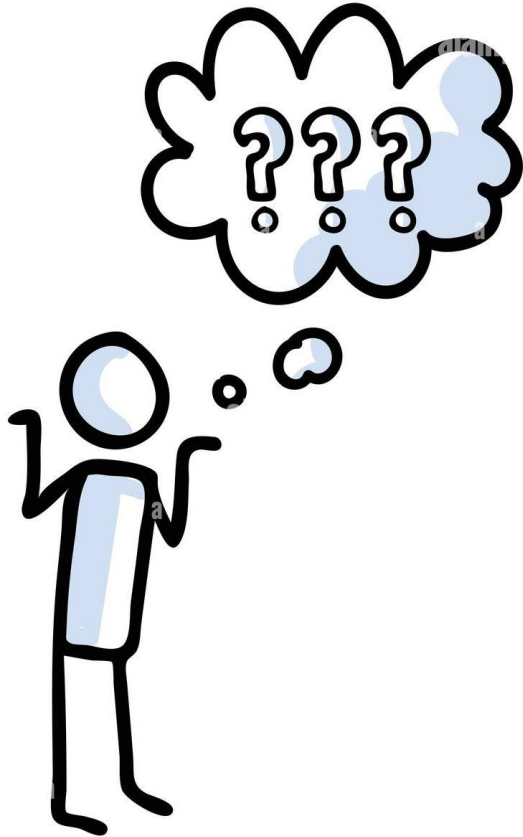


CLINICAL CASE



	Aug 2005	Aug 2006	Nov 2008	Mar 2009	Nov 2014	Apr 2016
WBC	7.86 k/ μ L	7k/ μ L	15.8 k/ μ L	17.8k/ μ L	15.3 k/ μ L	16.4 k/ μ L
Hgb	18 g/dL	13.9 g/dL	12.8 g/dL	13.5 g/dL	11.5 g/dL	11 g/dL
PLTs	319 k/ μ L	554 k/ μ L	359 k/ μ L	413 k/ μ L	410 k/ μ L	334 k/ μ L
Hct	58%	44%	47%	43%	42.6%	43%
No of PHL/yr	4 (Aug-sep 2005)	6	3	1 (3 months)	0	0

CLINICAL CASE

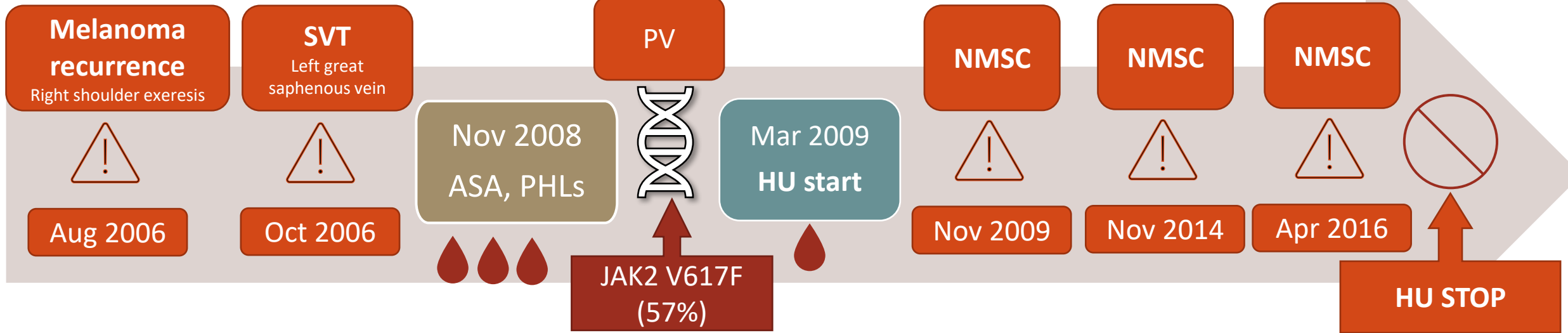


**Would you have
stopped HU?**

1. Yes
2. No

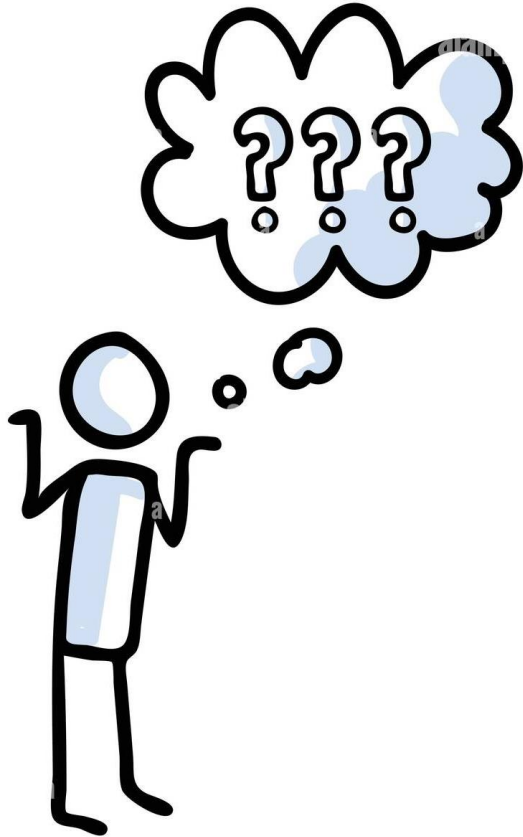


CLINICAL CASE



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No of PHL/yr	4 (Aug-sep 2005)	6	3	1 (3 months)	0	0

CLINICAL CASE

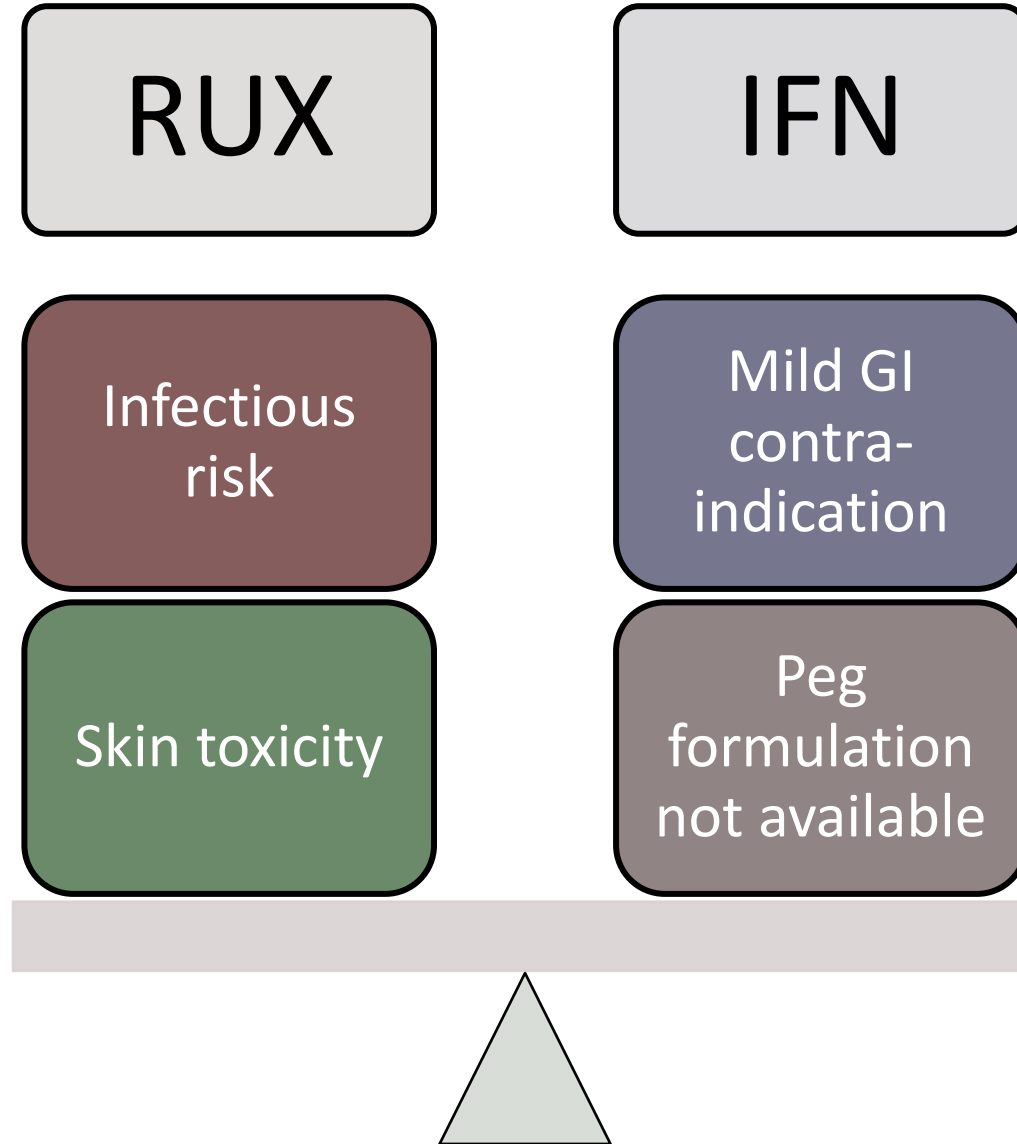


Which drug would you use now?

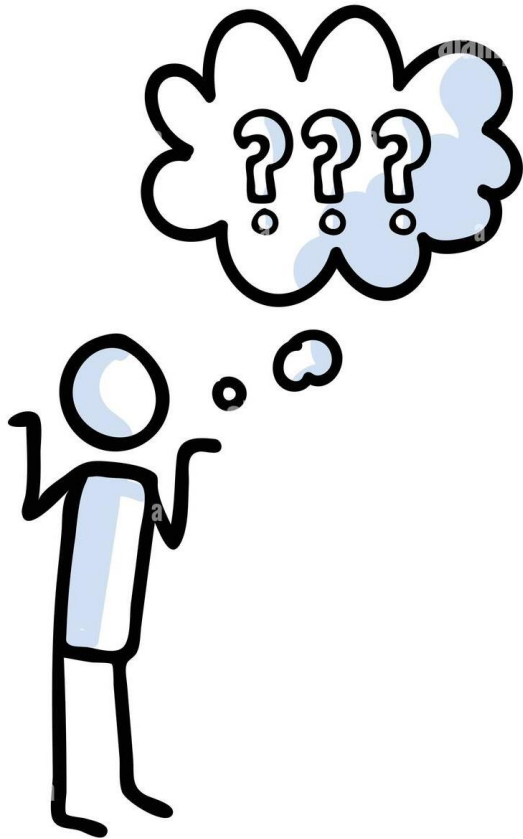
- 1. No cytoreduction needed**
- 2. Busulfan**
- 3. Ruxolitinib**
- 4. Interferon**



CLINICAL CASE



CLINICAL CASE

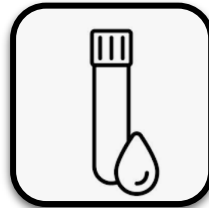


which drug would you have used?

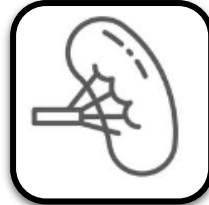
1. No cytoreduction needed
2. Busulfan
- 3. Ruxolitinib**
4. Interferon

CLINICAL CASE – May 2016

MEN 79 years-old– hypertension, IBD, multiple melanoma and NMSCs exeresis, recurrent superficial venous thrombosis, BPH, severe right arotid artery stenosis



WBCs $9.7 \times 10^9/L$ (normal differential count), Hb 15.3g/dl, Hct 46.7 % MCV 74 fl, PLT $471 \times 10^9/L$,



Spleen 13.5 cm, mild hepatosteatosi



Moderate fatigue

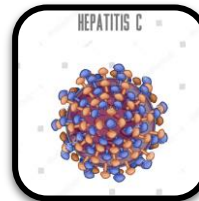


PV, fibrosis G0-1



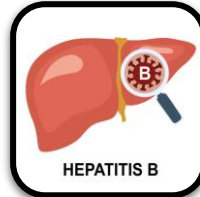
CLINICAL CASE – May 2016

Screening for RUX start



HEPATITIS C

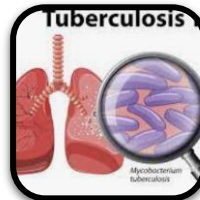
HCV IgG neg



HEPATITIS B

Anti Hbc pos
HBV DNA neg

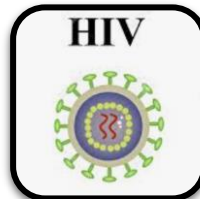
Lamivudine
prophylaxis



Tuberculosis

Mycobacterium tuberculosis

Quantiferon neg

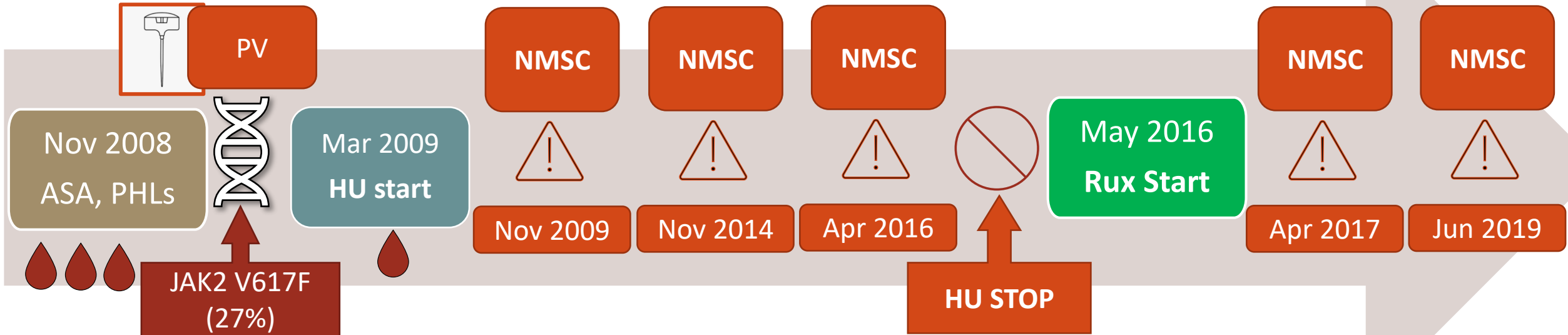


HIV

HIV neg

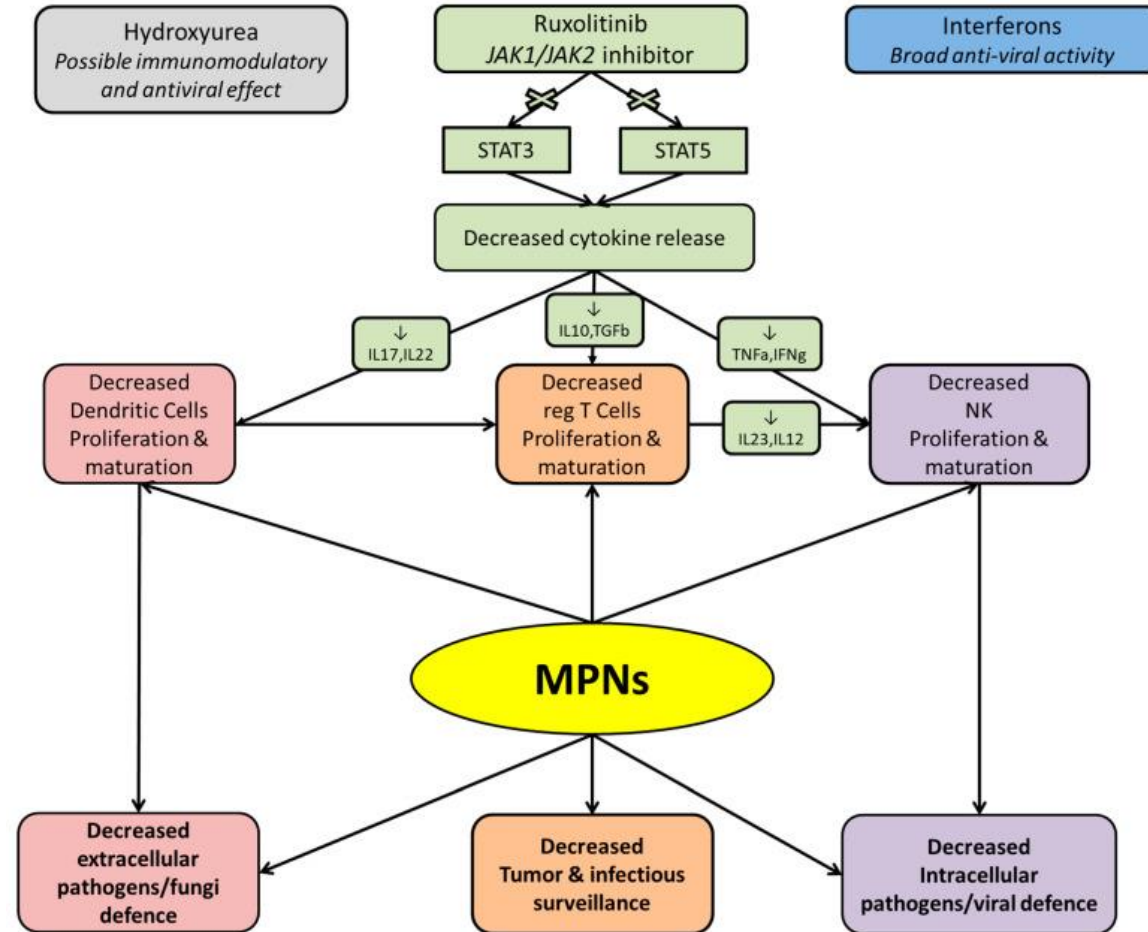


CLINICAL CASE



	Nov 2008	Mar 2009	Nov 2014	Apr 2016	Apr 2017	Jun 2019
WBC	15.8 k/ μ L	17.8k/ μ L	15.3 k/ μ L	16.4 k/ μ L	14.6 k/ μ L	15.6 k/ μ L
Hgb	12.8 g/dL	13.5 g/dL	13.1 g/dL	14 g/dL	12.6 g/dL	13.7 g/dL
PLTs	359 k/ μ L	413 k/ μ L	410 k/ μ L	334 k/ μ L	371 k/ μ L	260 k/ μ L
Hct	47%	43%	42.6%	45.7%	41.4%	38%
No of PHL/yr	3	1 (3 months)	0	0	0	0

POSSIBLE MECHANISMS UNDERLYING INCREASED SPM RISK DURING CYTOREDUCTIVE THERAPY



Palandri F, et al. Cancers (Basel). 2021 Sep 23;13(19):4750.



Second neoplasms in RUX-exposed PV patients

Response-2

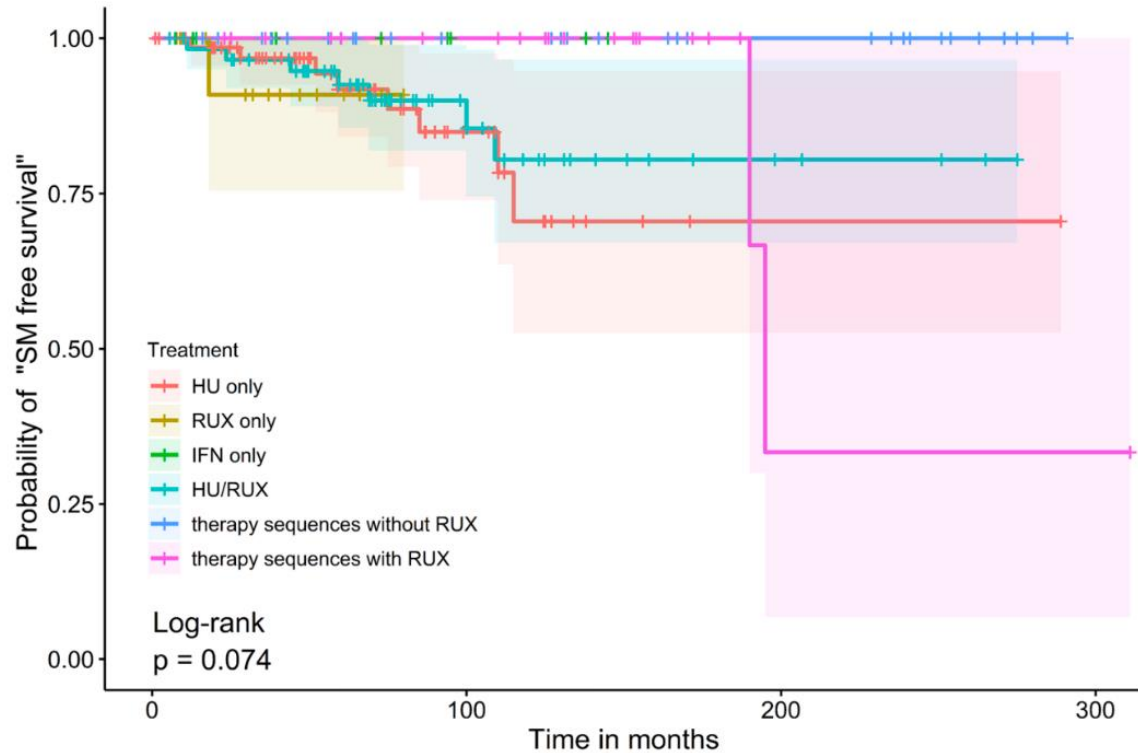
	Ruxolitinib group (n=74)				Best available therapy group (n=75)*				Crossover group (n=58)†			
	Any grade	Grade 1 or 2	Grade 3	Grade 4	Any grade	Grade 1 or 2	Grade 3	Grade 4	Any grade	Grade 1 or 2	Grade 3	Grade 4
Any adverse event	74 (22.1)	24 (7.2)	43 (12.9)	7 (2.1)	64 (120.0)	42 (78.7)	19 (35.6)	3 (5.6)	57 (27.7)	24 (11.7)	25 (12.1)	8 (3.9)
Adverse events of special interest‡												
Infections (excluding tuberculosis)§¶	49 (14.7)	42 (12.6)	7 (2.1)	0	18 (33.7)	16 (30.0)	1 (1.9)	1 (1.9)	31 (15.1)	26 (12.6)	3 (1.5)	2 (1.0)
Other infections	41 (12.3)	38 (11.4)	3 (0.9)	0	18 (33.7)	16 (30.0)	2 (3.7)	0	25 (12.1)	23 (11.2)	2 (1.0)	0
Erythropenia (anaemia)	29 (8.7)	29 (8.7)	0	0	3 (5.6)	2 (3.7)	1 (1.9)	0	20 (9.7)	18 (8.7)	2 (1.0)	0
Bleeding (haemorrhages)	22 (6.6)	18 (5.4)	4 (1.2)	0	8 (15.0)	7 (13.1)	1 (1.9)	0	16 (7.8)	14 (6.8)	2 (1.0)	0
Weight gain	19 (5.7)	17 (5.1)	2 (0.6)	0	1 (1.9)	1 (1.9)	0	0	9 (4.4)	9 (4.4)	0	0
Urinary tract infections	17 (5.1)	15 (4.5)	2 (0.6)	0	0	0	0	0	5 (2.4)	3 (1.5)	2 (1.0)	0
Malignant tumours	15 (4.5)	8 (2.4)	5 (1.5)	2 (0.6)	4 (7.5)	1 (1.9)	2 (3.7)	1 (1.9)	9 (4.4)	4 (1.9)	3 (1.5)	2 (1.0)
Hypertension	15 (4.5)	6 (1.8)	8 (2.4)	1 (0.3)	3 (5.6)	0	3 (5.6)	0	11 (5.3)	4 (1.9)	7 (3.4)	0

- Malignant tumours (any grade) were reported in 15 patients in the ruxolitinib group (4 considered treatment-related), in 9 patients who crossed over (2 treatment-related), and in 4 patients in the best available therapy group (two treatment related), with exposure-adjusted rates of 4.5%, 4.4%, and 7.5%, respectively.
- Non-melanoma skin cancer (any grade) was reported in 9 patients in the ruxolitinib group (4 treatment-related), in 6 patients who crossed over (2 treatment-related), and in 1 patient in the best available therapy (one treatment-related), with exposure-adjusted rates of 2.7%, 2.9%, and 1.9%, respectively.

Passamonti f et al. Lancet Haematol. 2022 Jul;9(7):e480-e492



Second neoplasms in RUX-exposed PV patients



Treatment	0	100	200	300
HU only	72 (0)	15 (6)	1 (8)	0 (8)
RUX only	13 (0)	0 (1)	0 (1)	0 (1)
IFN only	11 (0)	2 (0)	0 (0)	0 (0)
HU/RUX	60 (0)	19 (6)	4 (7)	0 (7)
therapy sequences without RUX	30 (0)	19 (0)	11 (0)	0 (0)
therapy sequences with RUX	22 (0)	16 (0)	1 (2)	1 (2)

Number at risk (number of events)

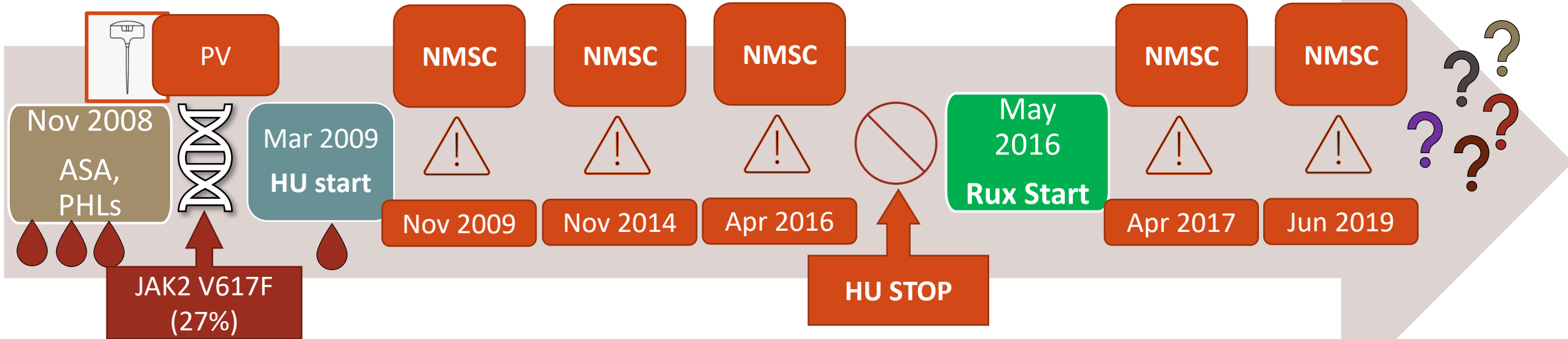
Time in months

- Retrospective, single-center study that included 289 PV patients. RUX was administered to 32.9% (95/289) of patients for a median treatment duration of 48.0 months.
- 63.6% of NMSC occurred in patients receiving RUX after HU pretreatment.
- No evidence of increased risk of secondary malignancies, particularly lymphoma, in PV patients treated with RUX

It is most likely that there is a correlation between the development of NMSC and HU pretreatment.

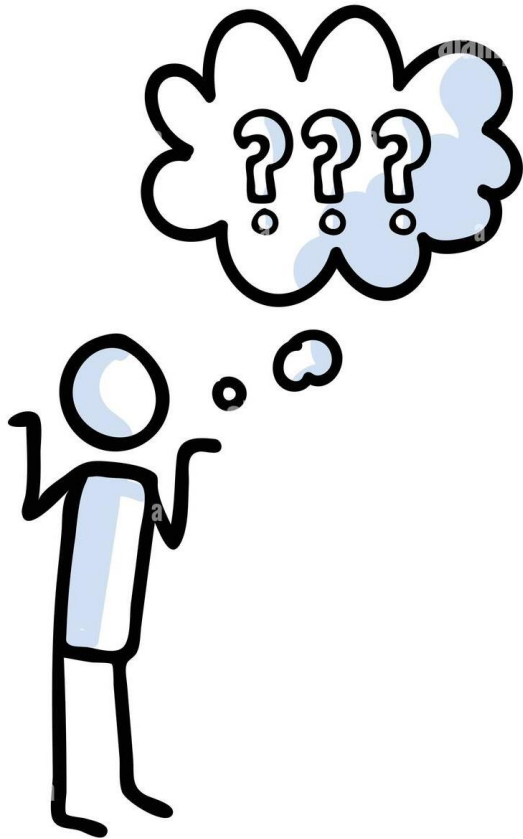
Sekhri R, et al. *Ann Hematol.* 2021 Nov;100(11):2707-2716

CLINICAL CASE



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No of PHL/yr	3	1 (3 months)	0	0	0	0

CLINICAL CASE

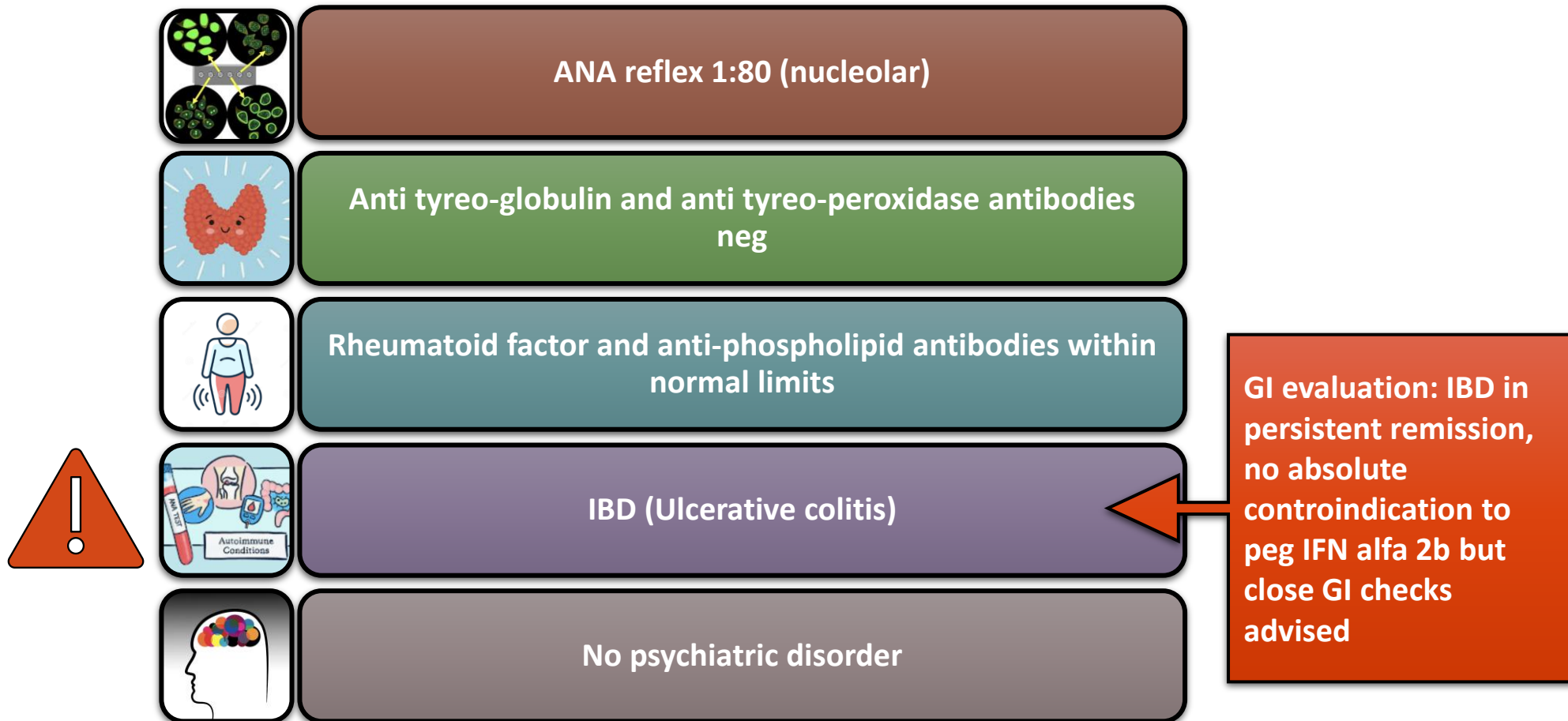


What about now?

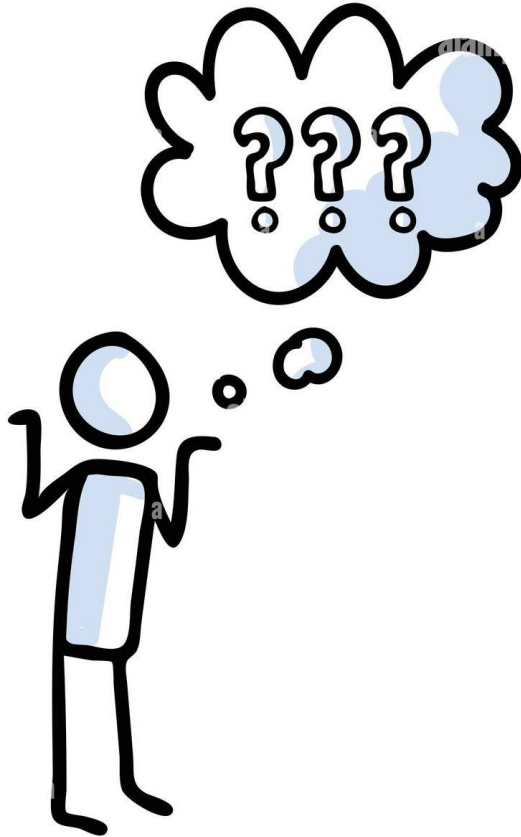
1. Continue RUX and intensify dermatologic fu
2. Start Peg-rIFN-a
3. Back to HU
4. Only phebotomies

CLINICAL CASE

Screening for Peg-rIFN-a start



CLINICAL CASE

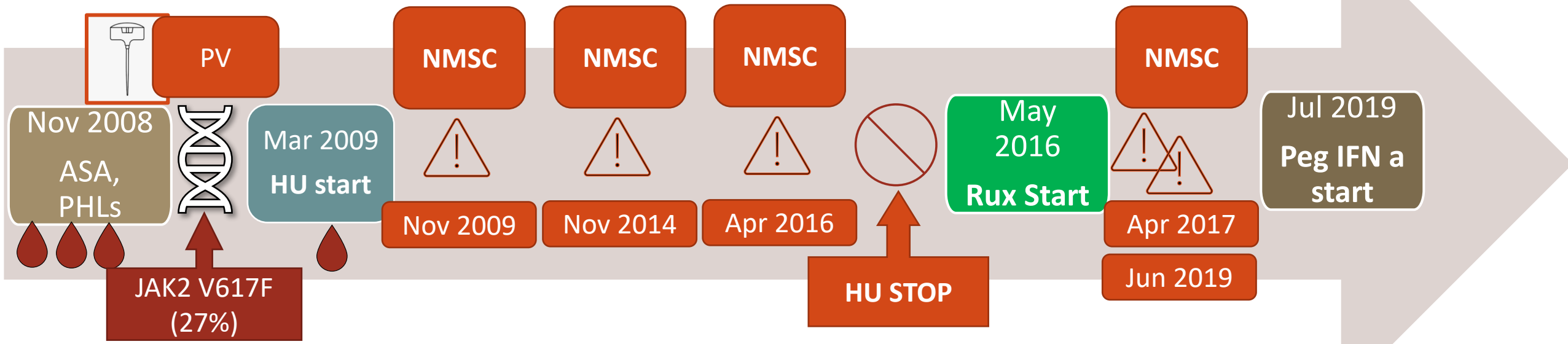


What about now?

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- 2. Start Peg-rIFN-a**
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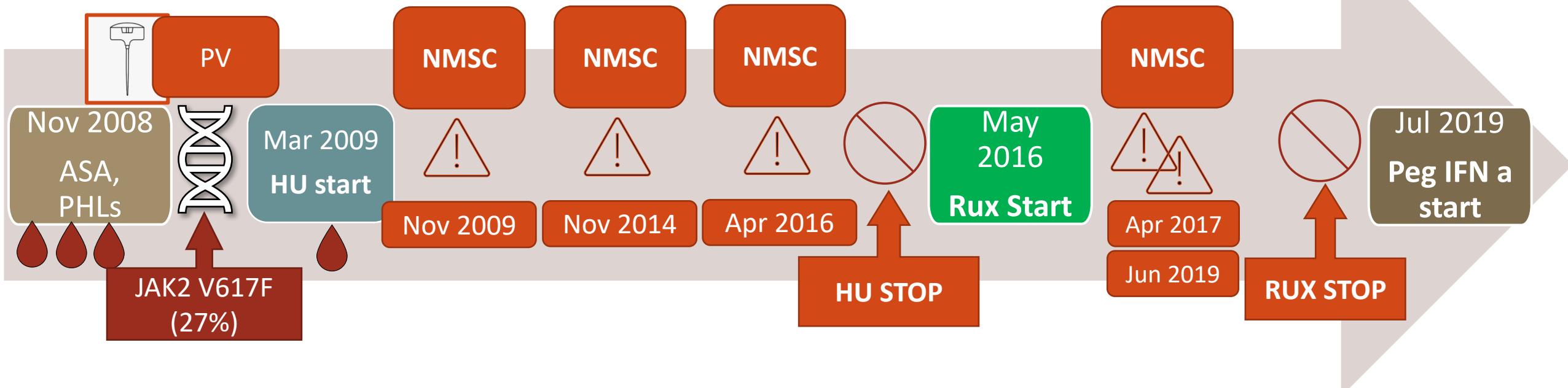
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No of PHL/yr	3	1 (3 months)	0	0	0	0



CLINICAL CASE



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WBC	15.8 k/ μ L	17.8k/ μ L	15.3 k/ μ L	16.4 k/ μ L	14.6 k/ μ L	15.6 k/ μ L	9.4k/ μ L
Hgb	12.8 g/dL	13.5 g/dL	13.1 g/dL	14 g/dL	12.6 g/dL	13.7 g/dL	11.5 g/dL
PLTs	359 k/ μ L	413 k/ μ L	410 k/ μ L	334 k/ μ L	371 k/ μ L	260 k/ μ L	180 k/ μ L
Hct	47%	43%	42.6%	45.7%	41.4%	44.7%	38.2%
No of PHL/yr	3	1 (3 months)	0	0	0	0	0

Feb 2021
 Peg IFN alfa 2 b ongoing, no side effects
 Still stable IBD





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